

We claim:

1. A method for determining whether an agent is capable of inhibiting the aggregation of  $\alpha$ -synuclein, comprising:

(a) adding said agent to a sample containing  $\alpha$ -synuclein in the presence of exogenous iron or copper, and allowing the  $\alpha$ -synuclein to aggregate;

(b) determining the amount, if any, of aggregated  $\alpha$ -synuclein; and

(c) comparing the amount from step (b) with an amount determined in a control sample wherein said agent is absent,

wherein a decrease in the amount of aggregated  $\alpha$ -synuclein indicates that the agent is capable of inhibiting the aggregation of  $\alpha$ -synuclein.

2. The method of claim 1, wherein free radical generator(s) is added to the sample in step (a) to assist in the aggregation of  $\alpha$ -synuclein.

3. The method of claim 1, wherein in step (a) exogenous iron is added.

4. The method of claim 2, wherein the free radical generator is dopamine or hydrogen peroxide.

5. The method of claim 1, wherein the sample is composed of cells that over-express  $\alpha$ -synuclein.

6. The method of claim 5, wherein the cells are of neuronal origin.

7. The method of claim 1, wherein the amount of aggregation is determined by protein separation, whereby the aggregated material displays a higher molecular weight than unaggregated  $\alpha$ -synuclein.

8. The method of claim 7, wherein the protein separation is accomplished by gel electrophoresis.

5 9. The method of claim 1, wherein the amount of aggregation is determined by adding a labeled anti- $\alpha$ -synuclein antibody and measuring the bound label.

10. The method of claim 9, wherein the label is a peroxidase.

10 11. The method of claim 1, wherein the amount of aggregation is determined by binding to thioflavine-S.

12. A kit for testing affects of substances on aggregation of  $\alpha$ -synuclein, comprising lyophilized  $\alpha$ -synuclein, iron or copper salt, and a buffer.

15 13. The kit of claim 12, which comprises iron chloride.

14. The kit of claim 12, which further comprises a free radical generator.

20 15. The kit of claim 14, wherein the free radical generator is hydrogen peroxide.

25 16. A method for treating a neurodegenerative disease that involves the formation of Lewy bodies, comprising administering to a patient in need thereof one or more agents that inhibit the formation of  $\alpha$ -synuclein aggregates, whereby the presence of Lewy bodies remains the same or is reduced.

17. The method of claim 16, wherein the agent is  $\text{Mg}^{2+}$ .

30 18. The method of claim 17, wherein the agent is  $\text{MgSO}_4$ .

19. The method of claim 16, wherein the agent is a peptide that binds to  $\alpha$ -synuclein and inhibits the aggregation thereof.

20. The method of claim 19, wherein said peptide binds to any part of the C-terminal amino acids 113 - 140, or the NAC (non-amyloid- $\beta$  protein component) portion of  $\alpha$ -synuclein.

21. The method of claim 20, wherein the peptide is selected from the group consisting of: WRQTRKD; HYAKNPI; ATINKSL; RRRGMAI; THRLPSR; TKHGPRK; SLKRLPK; RLRGRNQ; WPFHHHR; HLYHHKT; THHHPS; and MMMMMRL.

22. The method of claim 21, wherein the peptide is selected from the group consisting of: THRLPSR; SLKRLPK; THHHPS; and MMMMMRL.

23. The method of claim 22, wherein the peptide is SLKRLPK.

24. The method of claim 16, wherein the agent is a composition containing  $Mg^{2+}$  in combination with a peptide.

25. The method of claim 24, wherein the agent is selected from the group consisting of: WRQTRKD; HYAKNPI; ATINKSL; RRRGMAI; THRLPSR; TKHGPRK; SLKRLPK; RLRGRNQ; WPFHHHR; HLYHHKT; THHHPS; and MMMMMRL.

26. The method of claim 25, wherein the agent is selected from the group consisting of: THRLPSR; SLKRLPK; THHHPS; and MMMMMRL.

27. The method of claim 26, wherein the peptide is SLKRLPK.

28. The method of claim 16, wherein the neurodegenerative disease

is Parkinson's disease, Alzheimer's disease diffuse Lewy body disease, mixed AD-PD, multiple system atrophy and Hallervorden-Spatz disease.

29. The method of claim 28, wherein the neurodegenerative disease is Parkinson's disease.

30. A method for inhibiting the formation of aggregates of  $\alpha$ -synuclein, comprising treating the  $\alpha$ -synuclein with a substance containing  $Mg^{2+}$ .

31. A method for inhibiting the formation of aggregates of  $\alpha$ -synuclein, comprising treating the  $\alpha$ -synuclein with a peptide that binds to  $\alpha$ -synuclein and inhibits the aggregation thereof.

32. The method of claim 30, wherein the substance further comprises at least one peptide that binds to  $\alpha$ -synuclein and inhibits the aggregation thereof.

33. A composition comprising  $Mg^{2+}$  and at least one peptide which binds to  $\alpha$ -synuclein and inhibits the aggregation thereof.

34. The composition of claim 33, wherein the peptide binds to the C-terminal or the NAC portion of  $\alpha$ -synuclein.

35. The composition of claim 34, wherein the peptide is selected from the group consisting of: WRQTRKD; HYAKNPI; ATINKSL; RRRGMAI; THRLPSR; TKHGPRK; SLKRLPK; RLRGRNQ; WPFHHHR; HLYHHKT; THIHHP; and MMMMRL.

36. The composition of claim 35, wherein the peptide is selected from the group consisting of: THRLPSR; SLKRLPK; THIHHP; and MMMMRL.

37. The composition of claim 36, wherein the peptide is SLKRLPK.

38. The composition of claim 33, wherein the  $Mg^{2+}$  is  $MgSO_4$ .

39. A peptide that will bind to  $\alpha$ -synuclein and inhibit its aggregation.

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40. The peptide of claim 39, wherein the peptide comprises a sequence selected from the group consisting of: WRQTRKD; HYAKNPI; ATINKSL; RRRGMAI; THRLPSR; TKHGPRK; SLKRLPK; RLRGRNQ; WPFHHHR; HLYHHKT; THHHPS; and MMMMMRL.

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41. The peptide of claim 40, wherein the peptide comprises a sequence selected from the group consisting of: THRLPSR; SLKRLPK; THHHPS; and MMMMMRL.

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42. The peptide of claim 41, which comprises the sequence SLKRLPK.

43. A composition comprising the peptide of claim 39, and a pharmaceutically acceptable carrier.

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44. The composition of claim 43, which comprises a peptide containing a sequence selected from the group consisting of: WRQTRKD; HYAKNPI; ATINKSL; RRRGMAI; THRLPSR; TKHGPRK; SLKRLPK; RLRGRNQ; WPFHHHR; HLYHHKT; THHHPS; and MMMMMRL.

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45. The composition of claim 44, which comprises a peptide containing a sequence selected from the group consisting of: THRLPSR; SLKRLPK; THHHPS; and MMMMMRL.

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46. The composition of claim 45, which comprises a peptide containing the sequence SLKRLPK.

47. A method for identifying peptides that are useful for inhibiting the aggregation of  $\alpha$ -synuclein, comprising:

(a) binding an  $\alpha$ -synuclein C-terminal or NAC portion peptide to a solid substrate;

5 (b) adding a phage display library of random peptides, and allowing binding to take place with the  $\alpha$ -synuclein;

(c) detecting any bound phage; and

(d) determining which peptide is displayed on bound phage, whereby such a peptide is useful for inhibiting aggregation of  $\alpha$ -synuclein.

10 48. The method of claim 47, wherein the  $\alpha$ -synuclein peptide contains amino acids 121 - 131 of  $\alpha$ -synuclein.

15 49. The method of claim 47, wherein the  $\alpha$ -synuclein peptide contains amino acids 61-87 of  $\alpha$ -synuclein.

50. The method of claim 47, wherein the peptides of the phage display library are seven amino acids in length.

20 51. A method for determining whether an agent is capable of inhibiting the aggregation of  $\alpha$ -synuclein, comprising:

(a) labelling  $\alpha$ -synuclein with a fluorescent label, and mixing labelled and unlabelled  $\alpha$ -synuclein in solution with an agent suspected of being inhibitory to  $\alpha$ -synuclein aggregation, and allowing the  $\alpha$ -synuclein to aggregate;

25 (b) determining the amount, if any, of aggregation of  $\alpha$ -synuclein by monitoring changes in the anisotropy of the solution by observing changes in the polarization of the solution; and

30 (c) comparing the amount from step (b) with an amount determined in a control sample wherein said agent is absent,

wherein changes in the polarization indicate aggregation has occurred, and wherein an observed decrease in the amount of aggregation in the presence of the agent indicates that the agent is capable of inhibiting the aggregation of  $\alpha$ -synuclein.